UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,903	11/20/2001	Emad S. Alnemri	480140.434D1	1791

500 7590 03/03/2003

SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 6300
SEATTLE, WA 98104-7092

EXAMINER	
NICKOL, GARY B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/03/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,903	ALNEMRI ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

In response to the preliminary amendment (Paper No. 10) filed April 8, 2002:

Claims 1-55 were cancelled.

Claims 56-64 were added and are currently pending.

Specification

The specification is objected to for the following reason: The specification on page 1 should be amended to reflect the priority status of the present application, for example, applicant should indicate that US Application No. 09/139,600 is now U.S. Patent No. 6432628.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibody or an antigen binding fragment thereof specific for a caspase-14 polypeptide comprising SEQ ID NO. 2 (Claim 56) or SEQ ID NO:5 (Claim 61) does not reasonably provide enablement for an isolated antibody or an antigen binding fragment thereof specific for a caspase-14 polypeptide, wherein said polypeptide comprises a polypeptide sequence having greater than 80% identity with SEQ ID NO. 2 or alternatively, with SEQ ID NO:5. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to isolated antibodies or antigen binding fragments thereof specific for a polypeptide having greater than 80% identity with SEQ ID NO:2 or SEQ ID NO:5; an isolated cell expressing said antibodies; antibodies which are polyclonal or monoclonal; and antigen binding fragments comprising an Fv portion of the antibody.

This includes a whole universe of antibodies specific for a whole universe of polypeptides with greater than 80% identity to SEQ ID NO.2 or SEQ ID NO:5. This further includes a whole universe of antibodies which bind to undefined sequences (i.e. those that recognize epitopes in the remaining 20% of polypeptides encompassed by the invention).

The specification teaches (page 9, lines 26+) that a caspase-14 polypeptide includes polypeptides having substitutions of conserved and non-essential amino acids of SEQ ID Nos: 2 or 5 and, generally includes, for example, mammalian homologues of SEQ ID Nos: 2 or 5 such as rat or other mammalian caspase-14. The specification further teaches that caspase-14 polypeptides include polypeptides having related but different sequences, provided the polypeptide has at least one functional activity of SEQ ID Nos: 2 or 5, such as protease activity.

The specification further teaches (page 10, lines 10+) that limited modifications may be made to a caspase-14 polypeptide without destroying its biological function wherein such modifications may be deliberate or accidental and that it is also understood that allelic variants and splice variants of caspase-14 are encompassed by the invention.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to any antibody including those that recognize amino acid sequences unrelated to a caspase-14 polypeptide, (i.e. epitopes that encompass the remaining 20% of polypeptides for which the invention is drawn) and those that bind polypeptides with greater than 80% sequence identity to SEQ ID Nos: 2 or 5 with or without the biological properties representative of a caspase-14 polypeptide, and applicant has not enabled all of these types of modified proteins because it has not been shown that these modified proteins are capable of functioning as that which is being disclosed.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990, IDS). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988, IDS). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the

specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, IDS). Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to use any and all antibodies that are specific for polypeptide fragments with greater than 80% sequence similarity to the amino acid sequences of SEQ ID NO. 2 and 5. Therefore, in view of the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 56-64 are rejected under 35 U.S.C. 102(e) as being anticipated by Ni *et al.* (US Patent No. 5,840,509; July 22, 1996).

Ni *et al.* teach an isolated antibody or an antigen binding fragment thereof specific for an ICE related protease. In a broad interpretation, claims 56 and 61 read on any antibody that binds to an epitope of any amino acid sequence since 20% of the claimed polypeptide structure is undefined. Accordingly, the antibody of Ni *et al.* clearly anticipates the claimed invention. Ni *et al.* further teach wherein said antibody is polyclonal or monoclonal (column 22); wherein said antigen binding fragment comprises an Fv portion (column 21) and an isolated cell expressing the antibody (column 22).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 61-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rasmussen *et al.* (Electrophoresis, Vol. 13, pages 960-969, 1992).

Rasmussen *et al.* teach an isolated polypeptide comprising a polypeptide sequence having greater than 80% identity with SEQ ID NO:5 (see attached sequence comparison at the end of this action).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce an isolated antibody such as monoclonal antibodies to the antigen identified by Rasmussen *et al.* because the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of monoclonals antibodies against it is *prima facie* obviuos. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. APp. & Int. 1990). Thus, to make such antibodies, it would have been further obvious to include an isolated cell expressing the monoclonal antibody because the manufacture of such antibodies by the use of tumor-fused spleen cells to produce hybridomas was well known to those of ordinary skill at the time the article was published. It would have been further *prima facie* obvious to one of ordinary skill in

the art at the time the invention was made to produce polyclonal antibodies by immunization techniques for the purposes of isolating and studying the expressed protein as well as producing antigen binding fragments that comprise an Fv portion because the use of such polyclonal antibodies and truncated portions thereof are well-known and conventional in the art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
February 28, 2003